

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 884

[Docket No. 99N-0922]

DMP

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Obstetrics and Gynecology Devices; Proposed Requirement for Premarket Approval and Change in Classification of Glans Sheath Devices

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the glans sheath medical device. The agency is also summarizing its proposed findings regarding the degree of risk of illness or injury intended to be eliminated or reduced by requiring the device to meet the statute's approval requirements as well as the benefits to the public from the use of the device. In addition, FDA is announcing the opportunity for interested persons to request the agency to change the classification of the device based on new information. This action is being taken to establish that there is sufficient information to provide reasonable assurance of the safety and effectiveness of this type of device.

DATES: Written comments by (*insert date 90 days after date of publication in the Federal Register*); requests for a change in classification by (*insert date 15 days after date of publication in the Federal Register*).

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ADDRESSES: Submit written comments or requests for a change in classification to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Colin M. Pollard, Center for Devices and Radiological Health (HFZ-470), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-594-1180.

SUPPLEMENTARY INFORMATION:

I. Background

Section 513 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c) requires the classification of medical devices into one of three regulatory classes: Class I (general controls), class II (special controls), and class III (premarket approval). Generally, devices that were on the market before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976 (the amendments) (Pub. L. 94-295), and devices marketed on or after that date that are substantially equivalent to such devices have been, or are being, classified by FDA. For convenience, this preamble refers to both the devices that were on the market before May 28, 1976, and the substantially equivalent devices that were marketed on or after that date as “preamendments devices.”

Section 515(b)(1) of the act (21 U.S.C. 360e(b)(1)) establishes the requirement that a preamendments device that FDA has classified into class III is subject to premarket approval. A preamendments class III device may be commercially distributed without an approved PMA or a notice of completion of a PDP until 90 days after the effective date of the final rule FDA issues requiring premarket approval for the device, or 30 months after final classification of the device, whichever is later. Also, a preamendments device subject to the rulemaking procedure under section 515(b) of the act is not required to have an approved investigational device exemption (IDE) (part 812 (21 CFR part 812)) contemporaneous with its interstate distribution until the date identified by FDA in the final rule requiring the submission of a PMA or PDP for the device. At that time,

an IDE must be submitted only if a PMA has not been submitted or a PDP has not been declared completed.

Section 515(b)(2)(A) of the act provides that a proceeding to issue a final rule to require premarket approval shall be initiated by publication of a notice of proposed rulemaking containing: (1) The proposed rule, (2) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device, (3) an opportunity to submit comments on the proposed rule and the proposed findings, and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

Section 515(b)(2)(B) of the act provides that if FDA receives a request for a change in the classification of the device within 15 days of the publication of the notice, FDA shall, within 60 days of the publication of the notice, consult with the appropriate FDA advisory committee and publish a notice denying the request for change of classification or announcing its intent to initiate a proceeding to reclassify the device under section 513(e) of the act. If FDA does not initiate such a proceeding, section 513(b)(3) of the act provides that FDA shall, after the close of the comment period on the proposed rule and consideration of any comments received, issue a final rule to require premarket approval, or publish a notice terminating the proceeding. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the act, unless the reason for termination is that the device is a banned device under section 516 of the act (21 U.S.C. 360f).

If a proposed rule to require premarket approval for a preamendments device is made final, section 501(f)(2)(B) of the act (21 U.S.C. 351(f)(2)(B)) requires that a PMA or a notice of completion of a PDP for any such device be filed within 90 days after the effective date of the final rule or 30 months after FDA's final classification of the device under section 513 of the act, whichever is later. If a PMA or a notice of completion of a PDP is not filed by the later

of the two dates, commercial distribution of the device is required to cease. The device may, however, be distributed for investigational use if the manufacturer, importer, or other sponsor of the device complies with the IDE regulations. If a PMA or a notice of completion of a PDP is not filed by the later of the two dates, and no IDE is in effect, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the act, and subject to seizure and condemnation under section 304 of the act (21 U.S.C. 334) if its distribution continues. Shipment of the device in interstate commerce will be subject to injunction under section 302 of the act (21 U.S.C. 332), and the individuals responsible for such shipment will be subject to prosecution under section 303 of the act (21 U.S.C. 333). In the past, FDA has requested that manufacturers take action to prevent the further use of devices for which no PMA has been filed and may determine that such a request is appropriate for the glans sheath device.

The act does not permit an extension of the 90-day period after the effective date of the final rule, within which an application or a notice is required to be filed. The House Report on the amendments states that “the thirty month ‘grace period’ afforded after classification of a device into class III * * * is sufficient time for manufacturers and importers to develop the data and conduct the investigations necessary to support an application for premarket approval” (H. Rept. 94-853; 94th Cong., 2d sess. 42 (1976)).

The Safe Medical Devices Act of 1990 (the SMDA) added section 515(i) to the act requiring FDA to review the classification of preamendments class III devices for which no final rule has been issued requiring the submission of PMA’s and to determine whether or not each device should be reclassified into class I or class II or remain in class III. For devices remaining in class III, the SMDA directed FDA to develop a schedule for issuing regulations to require premarket approval. The SMDA does not, however, prevent FDA from proceeding immediately to rulemaking under section 515(b) of the act on specific devices, in the interest of public health, independent of the procedures of section 515(i) of the act. Indeed, proceeding directly to rulemaking under section 515(b) of the act is consistent with Congress’ objective in enacting section 515(i) of the

act, i.e., that preamendments class III devices for which PMA's or notices of completed PDP's have not been required either be reclassified to class I or class II or be subject to the requirements of premarket approval. Moreover, in this proposal, interested persons are being offered the opportunity to request reclassification of glans sheath devices.

A. Classification of the Glans Sheath Device(s)

In the **Federal Register** of December 29, 1994 (59 FR 67185), FDA issued a final rule classifying glans sheath devices into class III. The preamble to the proposal to classify these devices (57 FR 42908, September 17, 1992) included the recommendation of the Obstetrics-Gynecology Devices Panel (the Panel), an FDA advisory committee, which met on March 7, 1989, regarding the classification of these devices (Ref. 1). During that meeting, the Panel concluded that “glans cap” devices, whose generic description FDA later changed to glans sheath devices (59 FR 67185), were a different type of generic device than were condom devices classified at 21 CFR 884.5300. The Panel recommended that glans sheath devices be classified into class III, and identified certain risks to health presented by the devices. The Panel believed that the devices presented a potential unreasonable risk to health and that insufficient information existed to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the devices or that application of special controls would provide such assurance.

FDA agreed with the Panel's recommendations and proposed that glans sheath devices be classified into class III (57 FR 42908). The proposal stated that FDA believed that general controls, or special controls, such as postmarket surveillance, the development of guidelines, the establishment of a performance standard, or other actions, are insufficient to provide reasonable assurance of the safety and effectiveness of the devices. The proposal stated that FDA believes that such devices present a potential unreasonable risk of illness or injury and that, in the absence of valid scientific evidence in the literature from published studies or test and clinical data that demonstrate the biocompatibility of materials, or that measure performance characteristics, such

as slippage, bursting, and tearing, the devices should be subject to premarket approval to ensure the safety and effectiveness of the devices.

In the **Federal Register** of January 6, 1989 (54 FR 550), FDA published a notice of intent to initiate proceedings to require premarket approval for 31 class III preamendments devices. Among other items, the notice described the factors FDA takes into account in establishing priorities for proceedings under section 515(b) of the act for issuing final rules requiring that preamendments class III devices have approved PMA's or declared completed PDP's. In the **Federal Register** of May 6, 1994 (59 FR 23731), FDA issued a notice of availability of a preamendments class III devices strategy document which updated its priorities and set forth the agency's plans for implementing the provisions of section 515(i) of the act for preamendments class III devices for which FDA had not yet required PMA approval. Although glans sheath devices were not included in the lists of devices identified in these notices and the strategy paper, using the factors set forth in these documents, FDA has recently determined that glans sheath devices identified in § 884.5320 (21 CFR 884.5320) have a high priority for initiating a proceeding for requiring premarket approval because the safety and effectiveness of these devices have not been established by valid scientific evidence as defined in (§ 860.7 (21 CFR 860.7)). Moreover, FDA believes that insufficient information exists to assess the safety and effectiveness of glans cap devices in preventing pregnancy and to derive reported failure or pregnancy rates based upon usage of the devices. FDA also believes that failure of the devices, which do not protect the shaft and foreskin of the penis against infection, may result in the release of infected semen into the vagina or otherwise result in the transmission of disease. Accordingly, FDA is commencing a proceeding under section 515(b) of the act to require that the glans sheath have an approved PMA or declared completed PDP.

B. Dates New Requirements Apply

In accordance with section 515(b) of the act, FDA is proposing to require that a PMA or a notice of completion of a PDP be filed with the agency for the glans sheath device within 90

days after the effective date of any final rule issued on the basis of this proposal. An applicant whose device was in commercial distribution before May 28, 1976, or whose device has been found by FDA to be substantially equivalent to such a device, will be permitted to continue marketing the glans sheath during FDA's review of the PMA or notice of completion of the PDP. FDA intends to review any PMA for the device within 180 days, and any notice of completion of a PDP for the device within 90 days of the date of filing. FDA cautions that, under section 515(d)(1)(B)(i) of the act, FDA may not enter into an agreement to extend the review period of a PMA beyond 180 days unless the agency finds that “* * * the continued availability of the device is necessary for the public health.”

FDA intends that, under § 812.2(d), the preamble to any final rule based on this proposal will state that, as of the date on which a PMA or a notice of completion of a PDP is required to be filed, the exemptions in § 812.2(c)(1) and (c)(2) from the requirements of the IDE regulations for preamendments class III devices will cease to apply to any glans sheath device which is: (1) Not legally on the market on or before that date; or (2) legally on the market on or before that date but for which a PMA or notice of completion of PDP is not filed by that date, or for which PMA approval has been denied or withdrawn.

If a PMA, notice of completion of a PDP, or an IDE application for a glans sheath device is not submitted to FDA within 90 days after the effective date of any final rule FDA may issue requiring premarket approval for the devices, commercial distribution of the devices must cease. FDA , therefore, cautions that for manufacturers not planning to submit a PMA or notice of completion of a PDP immediately, IDE applications should be submitted to FDA, at least 30 days before the end of the 90-day period after the effective date of the final rule that is published to minimize the possibility of interrupting all availability of the device. FDA considers investigations of glans sheath devices to pose a significant risk as defined in the IDE regulation.

C. Description of the Device

The glans sheath device is a sheath which covers only the glans penis or part thereof, and may also cover the area in the immediate proximity thereof, the corona and frenulum, but not the entire shaft of the penis. It is indicated only for the prevention of pregnancy and not for the prevention of sexually transmitted diseases (STD's).

FDA considers the use of glans sheath devices for preventing the transmission of STD's, such as, acquired immunodeficiency syndrome (AIDS) caused by the human immunodeficiency virus (HIV) from HIV-infected semen or vaginal secretions, to constitute investigational use of the device. Any glans sheath device in interstate commerce that is used, or that is labeled or promoted to be used, for preventing the transmission of STD's must already have in effect an approved IDE, or an approved PMA or declared completed PDP.

D. Proposed Findings with Respect to Risks and Benefits

As required by section 515(b) of the act, FDA is publishing its proposed findings regarding: (1) The degree of risk of illness or injury designed to be eliminated or reduced by requiring the glans sheath to have an approved PMA or a declared completed PDP, and (2) the benefits to the public from the use of the device.

E. Risk Factors

Glans sheath devices are associated with the following risks:

1. Pregnancy

Undesired pregnancy could occur if the device leaks, breaks, or dislodges during intercourse. For women for whom pregnancy is contraindicated due to medical conditions such as heart disease or diabetes mellitus, the risk of an unwanted pregnancy can be severe, even life threatening (Ref. 2). A search of the literature found no published studies or controlled clinical data which demonstrated the safety and effectiveness of the glans sheath device, or the expected failure or pregnancy rates for use of the glans sheath. Additionally, no testing or clinical study data were

available regarding leakage, breakage, or dislodgement of glans sheaths during intercourse.

References to this type of device in the literature described it as an unsafe method of contraception (Refs. 3 and 4).

2. Transmission of Diseases

If the device fails due to leakage, breakage, or dislodgement during intercourse, contact with infected semen or vaginal secretions containing infectious agents could result in the transmission of STD's, including AIDS, hepatitis B, cytomegalovirus infection, syphilis, and disseminated gonorrhea (Refs. 5 through 8). Organisms causing these systemic infections remain viable in the blood stream rendering almost all body fluids and semen infectious. The HIV virus causing AIDS has been isolated from infected blood, saliva, vaginal secretions, and semen. Semen from infected persons has been shown to be an important vehicle in spreading the disease (Refs. 5 through 8).

3. Adverse Tissue Reaction

Materials and substances that comprise the glans sheath could cause local tissue irritation and sensitization or systemic toxicity when the device contacts the glans penis or vaginal and cervical mucosa. Because of such intended contact, testing the biocompatibility of materials and substances that comprise the glans sheath is essential to provide reasonable assurance of the device's safety.

F. Benefits of the Device

The glans sheath covers only the glans penis or part thereof, and may also cover the area in the immediate proximity thereof, the corona and frenulum, so it may be acceptable to those individuals who would not otherwise use a full-sheath condom. The glans sheath may be an alternate preferred method of contraception which, arguably, may serve to increase penile stimulation by reducing the degree of interference and loss of sensitivity attributed to the use of contraceptives, in particular, in comparison to the use of full-sheath condoms. FDA has concluded from a review of the scientific literature that the safety and effectiveness of the glans sheath device

for contraceptive use for the prevention of pregnancy have not been established by valid scientific evidence as defined in § 860.7.

II. PMA Requirements

A PMA for the glans sheath device must include the information required by section 515(c)(1) of the act and § 814.20 (21 CFR 814.20) of the procedural regulations for PMA's. Such a PMA should include a detailed discussion of the risks as well as a discussion of the effectiveness of the device for which premarket approval is sought. In addition, a PMA must include all data and information on: (1) Any risks known, or that should be reasonably known, to the applicant that have not been identified in the proposal (57 FR 42908); (2) the effectiveness of the specific glans sheath that is the subject of the application; and (3) full reports of all preclinical and clinical information from investigations on the safety and effectiveness of the device for which premarket approval is sought.

A PMA should include valid scientific evidence as defined in § 860.7 and should be obtained from well-controlled clinical studies, with detailed data, in order to provide reasonable assurance of the safety and effectiveness of the particular glans sheath for its intended use. In addition to the basic requirements described in § 814.20(b)(6)(ii) for a PMA, it is recommended that such studies employ a protocol that meets the criteria described in the following paragraphs.

Applicants should submit any PMA in accordance with FDA's "Premarket Approval Manual." This manual is available on the world wide web at "<http://www.fda.gov/cdrh/dsma/manuals.html>".

A. General Protocol Requirements

Glans sheath devices should be evaluated in a prospective, randomized, clinical trial that uses adequate controls. The study must attempt to answer all of the questions concerning safety and effectiveness of the devices, including the risk to benefit ratio. The questions should relate to the

pathophysiologic effects which the devices produce, as well as the primary and secondary variables analyzed to evaluate safety and effectiveness. Study endpoints and study success must be defined.

Biocompatibility testing for new material and/or the finished devices should be performed according to the Office of Device Evaluation (ODE) blue book memorandum #G95-1 entitled “Use of International Standard ISO-10993, ‘Biological Evaluation of Medical Devices Part 1: Evaluation and Testing’” (Ref. 9). This memorandum includes the FDA-modified matrix that designates the type of testing needed for various medical devices. The memorandum is available upon request from CDRH’s Division of Small Manufacturers Assistance (address above) and is also available on the world wide web at “<http://www.fda.gov/cdrh/g951.html>”. The following tests should be considered: Cytotoxicity, sensitization, mucosal irritation, acute systemic toxicity, mutagenicity, and implantation (90 day).

Specific considerations include the following:

1. The selection of materials to be used in device manufacture and their toxicological evaluation should initially take into account a full characterization of the materials, such as chemical composition of components, known and suspected impurities, and processing. Any surface coatings to be applied are to be fully characterized, including materials, physical specifications, and application processes.
2. The materials of manufacture, the final product, and possible leachable chemicals or degradation products should be considered for their relevance to the overall toxicological evaluation of the devices.
3. Any in vitro or in vivo experiments or tests must be conducted according to recognized good laboratory practices followed by an evaluation by competent informed persons.
4. Any change in chemical composition, manufacturing process, physical configuration or intended use of the devices must be evaluated with respect to possible changes in toxicological effects and the need for additional testing.

5. The biocompatibility evaluation performed in accordance with the guidance should be considered in conjunction with other information from other nonclinical studies and postmarket experiences for an overall safety assessment.

Guidance concerning the type of information that should be provided regarding materials, finished product, processing, testing, and labeling may be found in the Office of Device Evaluation's draft guidance entitled "Testing Guidance For Male Condoms Made From New Material," June 29, 1995 (Ref. 10). This guidance is available upon request from CDRH's Division of Small Manufacturers Assistance and is also available on the world wide web at "<http://www.fda.gov/cdrh/ode/oderp455.html>". The following types of information should be provided:

1. The identity of resin manufacturers.
2. The chemical composition and specifications for raw materials, including molecular weight and molecular weight distribution, and a description of the quality control testing performed.
3. A complete description of the chemical composition and specifications for the finished device, including the molar ratio of component monomers for fabricating the finished material(s), physical characteristics (length, width, thickness, etc.).
4. The chemical composition and specifications for any retention ring materials, lubricants, or dusting agent.
5. Details on the processes used to manufacture the finished device to include: A flow diagram for all aspects of manufacturing and points where in-process quality assurance testing is performed, and descriptions of process control parameters, handling and/or reworking procedures for product that fails in-process quality assurance tests, procedures for adding lubricants and/or dusting agents, and packaging procedures.
6. Data from physical testing conducted on the finished device using appropriate sampling procedures and established performance limits and tolerances, to include tensile strength, force at break (vulnerability to puncture), elongation (elasticity), tear resistance, and other measures of flexural characteristics.

7. If a shelf-life period or expiration date is stated in device labeling, data from accelerated and/or real time testing of the packaged product, including lubricants and other agents, demonstrating the physical and mechanical integrity of the device for the shelf-life or expiration date period claimed in labeling.

8. Labeling providing: A complete description of the device, indications, adequate directions for use, and full disclosure of the safety and effectiveness findings from preclinical and clinical studies, including the recommended use of a pregnancy rate table and the disclosure that the product does not protect against HIV infection and other STD's. (See FDA guidance entitled "Uniform Contraceptive Labeling," July 23, 1998, which is available from CDRH's Division of Small Manufacturers Assistance (address above) and is also available on the world wide web at "<http://www.fda.gov/cdrh/ode/contrlab.html>".)

Examples of questions to be addressed by the clinical studies include, but are not limited to, the following:

1. What are the findings of preliminary studies conducted to evaluate the clinical performance (slippage and breakage) and the acceptability for use of the glans sheath device, including incidents of genital irritation or other adverse occurrences?

2. What breakage, slippage, partial slippage, dislodgement and adverse reaction data and rates are derived from the clinical trial(s) studying slippage and breakage, and what are the design and statistical analysis particulars of the trial(s), including whether the study followed a randomized, cross-over design and what patient population, inclusion/exclusion criteria, sample size, and statistical analysis models were chosen?

3. What pregnancy, breakage, slippage, and adverse event data and rates are derived from the clinical trial(s) evaluating the safety, effectiveness, and ease of use of the glans sheath device, and what are the design and statistical analysis particulars of the clinical study(ies), including whether the study(ies) followed a randomized controlled design, and what number of menstrual

cycles of product use, population size, inclusion/exclusion criteria, sample size, and statistical analysis models were chosen?

Statistically valid investigations should include a clear statement of the objectives, method of selection of subjects, nature of the control group, effectiveness and/or safety parameters, method of analysis, and presentation of statistical results of the study. Appropriate rationale, supported by background literature on previous uses of the particular glans sheath device and proposed mechanisms for its effect, should be presented as justification for the questions to be answered, and the definitions of study endpoints and success. Clear study hypotheses should be formulated based on this information.

B. Study Sample Requirements

The subject population should be well defined. Ideally, the study population should be as homogeneous as possible in order to minimize selection bias and reduce variability. Otherwise, a large population may be necessary to achieve statistical significance. Justification must be provided for the sample size used to show that a sufficient number of patients were enrolled to attain statistically and clinically meaningful results. Eligibility criteria for the subject population should include the subject's potential for benefit, the ability to detect a benefit in the subject, the absence of both contraindications and any competing risk, and assurance of subject compliance. In a heterogeneous sample, stratification of the patient groups participating in the multi-center clinical study may be necessary to analyze homogeneous subgroups and thereby minimize potential bias. All endpoint variables should be identified, and a sufficient number of patients from each subgroup analysis should be included to allow for stratification by pertinent demographic characteristics.

The investigations should include an evaluation of comparability between treatment groups and control groups (including historical controls). Baseline (e.g., age, gender, etc.) and other variables should be measured and compared between the treatment and control groups. The baseline variables should be measured at the time of treatment assignment, not during the course of the

study. Other variables should be measured during the study as needed to completely characterize the particular device's safety and effectiveness.

C. Study Design

All potential sources of error, including selection bias, information bias, misclassification bias, comparison bias, or other potential biases should be evaluated and minimized. The study should clearly measure any possible placebo effect. Treatment effects should be based on objective measurements. The validity of these measurement scales should be shown to ensure that the treatment effect being measured reflects the intended uses of the particular device.

Adherence to the protocol by subjects, investigators, and all other individuals involved is essential and requires monitoring to assure compliance by both patients and practitioners. Subject exclusion due to dropout or loss to followup greater than 20 percent may invalidate the study due to bias potential; therefore, initial patient screening and compliance of the final subject population will be needed to minimize the dropout rate. All dropouts must be accounted for and the circumstances and procedures used to ensure patient compliance must be well documented.

Endpoint assessment cannot be based solely on statistical value. Instead, the clinical outcome must be carefully defined to distinguish between the evaluation of the proper function of the device versus its benefit to the subject. Statistical significance and effectiveness of the device must be demonstrated by the statistical results. However, under certain restricted circumstances, a clinically significant result may be documented without statistical significance.

Observation of all potential adverse effects must be recorded and monitored throughout the study and the followup period. All adverse effects must be documented and evaluated.

D. Statistical Analysis Plan

The involvement of a biostatistician is recommended to provide proper guidance in the planning, design, conduct, and analysis of a clinical study. There must be sufficient documentation of the statistical analysis and results including comparison group selection, sample size justification,

stated hypothesis test(s), population demographics, study site pooling justification, description of statistical tests applied, clear presentation of data, and a clear discussion of the statistical results and conclusions.

In addition to this generalized guidance, the investigator or sponsor is expected to incorporate additional requirements necessary for a well-controlled scientific study. These additional requirements are dependent on what the investigator or sponsor intends to measure or what the expected treatment effect is based on each device's intended use.

E. Clinical Analysis

The analysis which results from the study should include a complete description of all the statistical procedures employed, including assumption verification, pooling justification, population selection, statistical model selection, etc. If any procedures are uncommon or derived by the investigator or sponsor for the specific analysis, an adequate description must be provided of the procedure for FDA to assess its utility and adequacy. Data analysis and interpretations from the clinical investigation should relate to the medical claims.

F. Monitoring

Rigorous monitoring is required to assure that the study procedures are collected in accordance with the study protocol. Attentive monitors, who have appropriate credentials and who are not aligned with patient management or otherwise biased, contribute prominently to a successful study.

III. PDP Requirements

A PDP for any of these devices may be submitted in lieu of a PMA and must follow the procedures outlined in section 515(f) of the act. A PDP should provide: (1) A description of the device; (2) preclinical trial information (if any); (3) clinical trial information (if any); (4) a description of the manufacturing and processing of the device; (5) the labeling of the device; and (6) all other relevant information about the device. In addition, the PDP must include progress reports and records of the trials conducted under the protocol on the safety and effectiveness of

the device for which the completed PDP is sought. FDA's current thinking on the PDP process and the relative duties and responsibilities of the agency and applicant is provided in the draft guidance entitled "Guidance for Industry—Contents of a Product Development Protocol; Draft." This draft guidance is available on the world wide web at "<http://www.fda.gov/cdrh/pdp/pdp.html>".

IV. Opportunity to Request a Change in Classification

Before requiring the filing of a PMA or a notice of completion of a PDP for a device, FDA is required by section 515(b)(2)(A)(i) through (iv) of the act and 21 CFR 860.132 to provide an opportunity for interested persons to request a change in the classification of the device based on new information relevant to its classification. Any proceeding to reclassify the device will be under authority of section 513(e) of the act.

A request for a change in the classification of the glans sheath device is to be in the form of a reclassification petition containing the information required by § 860.123 (21 CFR 860.123), including information relevant to the classification of the device, and shall, under section 515(b)(2)(B) of the act, be submitted by *(insert date 15 days after date of publication in the **Federal Register**)*.

The agency advises that, to ensure timely filing of any such petition, any request should be submitted to the Dockets Management Branch (address above) and not to the address provided in § 860.123(b)(1). If a timely request for a change in the classification of the glans sheath is submitted, FDA will, by *(insert date 60 days after date of publication in the **Federal Register**)* after consultation with the appropriate FDA advisory committee and by an order published in the **Federal Register**, either deny the request or give notice of its intent to initiate a change in the classification of the device in accordance with section 513(e) of the act and 21 CFR 860.130 of the regulations.

V. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Transcripts of the Obstetrics-Gynecology Devices Panel meeting, March 7, 1989.
2. Willson, J., and E. Carrington, *Obstetrics and Gynecology*, C. V. Mosby Co., chs. 22 and 27, 1987.
3. "Other Methods, Past, Present and Future * * * American, or Grecian Tips," in "Sex With Health The Which? Guide to Contraceptives, Abortion and Sex-related Diseases," published by Consumers' Association (British), November 1974.
4. Peel, J., and M. Potts, "The Condom," in "Textbook of Contraceptive Practice," Cambridge University Press, p. 58, 1969.
5. "Leads from the MMWR Morbidity and Mortality Weekly Report * * * 'Heterosexual Transmission of Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus,'" *Journal of the American Medical Association*, 254(15): pp. 2051 to 2054, 1985.
6. Winklestein, Jr., W. et al., "Sexual Practices and Risk of Infection by the Human Immunodeficiency Virus," *Journal of the American Medical Association*, 253(3): pp. 321 to 325, 1987.
7. Stone, K. M. et al., "Primary Prevention of Sexually Transmitted Diseases," *Journal of the American Medical Association*, 255(13): pp. 1763 to 1766, 1986.
8. Peterman, T. A., and J. W. Curran, "Sexual Transmission of Human Immunodeficiency Virus," *Journal of the American Medical Association*, 256(16): pp. 2222 to 2226, 1986.
9. "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing,'" ODE "Blue Book," General Program Memorandum #G95-1, FDA, Center for Devices and Radiological Health, Office of Device Evaluation, Rockville, MD 20857, May 1, 1995.

10. “Testing Guidance for Male Condoms Made From New Materials,” FDA, Center for Devices and Radiological Health, Office of Device Evaluation, Obstetrics–Gynecology Devices Branch, Rockville, MD 20857, June 29, 1995.

VI. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612) (as amended by subtitle D of the Small Business Regulatory Fairness Act of 1996 (Pub. L. 104–121) and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4)). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the proposed rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. FDA believes that only one firm, which previously distributed a glans sheath type of device in 1989, may be affected and required to submit a PMA at a cost of approximately \$1.2 million. However, because this type device has been classified into class III since December 29, 1994, and any manufacturer of this device that was legally in commercial distribution before May 28, 1976, or found by FDA to be substantially equivalent to such a device, will be permitted to continue marketing during FDA’s

review of the PMA or notice of completion of the PDP, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

VIII. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The burden hours required for § 884.5320(c) are included in the collection entitled “Premarket Approval of Medical Devices—21 CFR Part 814,” submitted on January 27, 1999 (64 FR 4112), for OMB approval.

IX. Submission of Comments with Data

Interested persons may, on or before (*insert date 90 days after date of publication in the Federal Register*), submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Interested persons may, on or before (*insert date 15 days after date of publication in the Federal Register*) submit to the Dockets Management Branch a written request to change the classification of the glans sheath. Two copies of any request are to be submitted except that individuals may submit one copy. Comments or requests are to be identified with the docket number found in brackets in the heading of this document. Received comments and requests may be seen in the office above between 9 a.m. and 4 p.m. Monday through Friday.

List of Subjects in 21 CFR Part 884

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 884 be amended as follows:

PART 884—OBSTETRICAL AND GYNECOLOGICAL DEVICES

1. The authority citation for 21 CFR part 884 continues to read as follows:

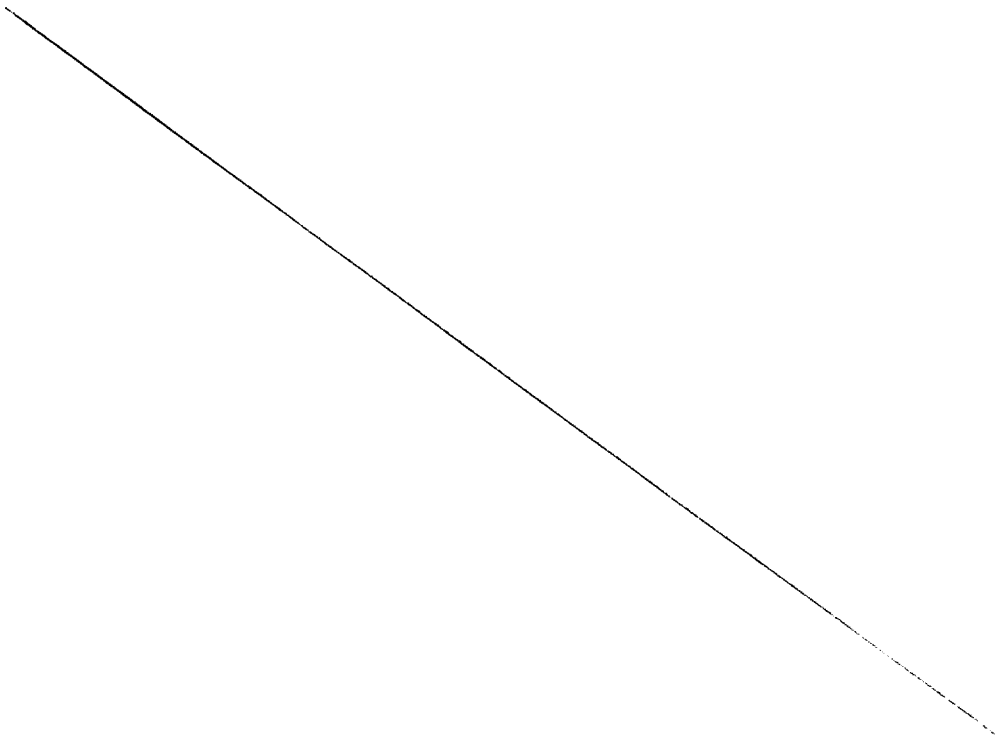
Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 884.5320 is amended by revising paragraph (c) to read as follows:

§ 884.5320 Glans sheath.

* * * * *

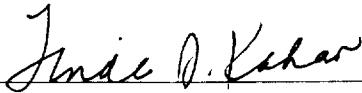
(c) *Date premarket approval application (PMA) or notice of completion of a product development protocol (PDP) is required.* A PMA or a notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before (date 90 days after date of publication of the final rule in the **Federal Register**), for any glans sheath that was in commercial distribution before May 28, 1976, or that has, on or before (date 90 days after date of publication of the final rule in the **Federal Register**) been found to be substantially equivalent to a glans



sheath that was in commercial distribution before May 28, 1976. Any other glans sheath shall have an approved PMA or a declared completed PDP in effect before being placed in commercial distribution.

Dated: 4/30/99

April 30, 1999



Linda S. Kahan
Deputy Director for
Regulations Policy
Center for Devices and
Radiological Health

[FR Doc. 99-???? Filed ??-??-99; 8:45 am]

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